REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

On October 20, 2004, a non-final Office Action was mailed to the Applicants. In this non-final Office Action claims 3-5, 14 and 17-39 were pending and rejected. A response to this non-final Office Action was filed on July 6, 2006 with a Petition for Revival of an Application for Patent Abandoned Unintentionally under 37 CFR 1.137(b). On July 27, 2006, the Petition for Revival was granted. On August 7, 2006, a Notice of Non-Compliant Amendment under 37 CFR 1.121 was mailed to the Applicants. This reply is in response to that notice.

By the present amendment, claim 32 has been amended and claims 20 and 21 have been canceled. It should be noted that when the application was originally filed, the application contained two claims designated as "claim 21." In the current amended form, both the first and second claim 21 have been canceled. Claim 40 has been added and is in the same form as the second claim 21. No new matter has been entered into the claims as a result of these amendments and entry thereof is respectfully requested.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 3-5, 14, 17-39 were rejected under 35 U.S.C. § 103(a) as being obvious over the combined disclosures of Cormier *et al.* (US 6,203,817) and Ke *et al.* (US 6,323,232). This rejection is traversed.

The Examiner stated that:

> The '817 patent discloses a transdermal formulation comprising an adhesive drug matrix reservoir (abstract). The transdermal [formulation] is attached to

> the skin and comprises a backing layer, adhesive overlay, and a release liner all sealed together to prevent leakage (col. 9, lin. 38-58). The formulation further comprises penetration enhancers (col. 10, lin. 5-56, examples). The transdermal formulation delivers various active agents including antiestrogen and antiosteoporotic agents such as tamoxifen and raloxifene (col. 7, lin. 66-68). The reference however lacks a disclosure of lasofoxifene a similar antiestrogen agent.
>
> And that:
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> The '232 patent discloses a combination transdermal therapy including lasofoxifene and other estrogen agonists/antagonists (claim 1). Among other agents used in combination therapy are droloxifene, raloxifene and tamoxifen (col. 6, lin. 35-40). A skilled artisan would have been motivated to include the lasofoxifene of '232 into the transdermal formulation of '817 in order to impart antiosteoporotic properties onto the formulation.
>
> And that:
>
> [O]ne of ordinary skill in the art would have been motivated to combine the teachings of '232 and '217 since both teach transdermal delivery of antiestrogen agents, in order to impart the antiosteoporotic properties of lasofoxifene onto the formulation.

To establish *a prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference(s) must teach or suggest all of the claim limitations. *See MPEP § 2142.*

When applying 35 U.S.C. § 103, four tenets of patent law must be adhered to: (1) the claimed invention must be considered as a whole; (2) the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (3) the references must be viewed without the benefit of impermissible hindsight vision; and (4) a reasonable expectation of success is the standard with which obviousness is determined. *See MPEP § 2141,* citing *Hodosh v. Block Drug Co., Inc.,* 786 F.2d 1136, 1143 (Fed. Cir. 1986).

Moreover, mere identification of each claimed element in the prior art is NOT sufficient to negate patentability. *In Re Rouffet,* 149 F.3d 1350, 1357 (Fed. Cir. 1998). Instead, there "must be a

teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the filed of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor." *ATD Corp. v. Lydall, Inc.,* 159 F.3d 534, 536 (Fed. Cir. 1998). Otherwise, sophisticated scientific fields would rarely, if ever, experience a patentable technical advance. *Rouffet,* 149 F.3d at 1357.

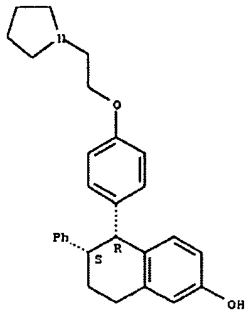
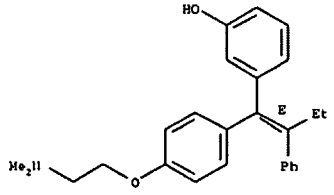
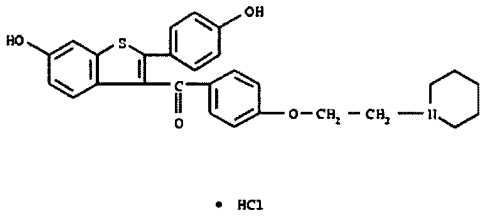
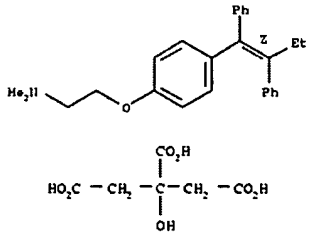
In this case, the Examiner has merely performed a database text search for some of the claimed elements and summarily rejected pending claims 3-5, 14, and 17-39 without discussing where each of the claimed elements are disclosed. The Examiner has also failed to explain where a motivation or suggestion is found demonstrating why one would be interested in combining these publications to arrive at the claimed invention.

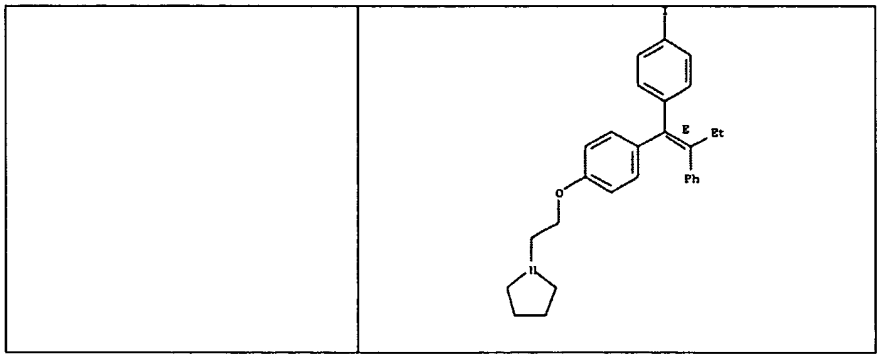
First, the Examiner asserts that Cormier *et al.* disclose a reservoir, backing layer, an adhesive overlay, a release liner and permeation enhancers for the delivery of raloxifene and tamoxifen. The Examiner's assertion, however, fails to address all of the claim elements. In regard to the transdermal formulation in independent claims 14, 32 and 36, the examiner has not provided publications describing claim elements such as the peel seal disc underlying the active agent permeable membrane, the heat seal about the periphery of the peel seal disc, the removable release liner, a free form hydroalcoholic gel, or a liquid reservoir formulation. As a result, the Examiner has not fulfilled one of the basic requirements for a *prima facie* case of obviousness since several claim elements are not accounted for in any of the publications cited. Therefore, in regard to the transdermal delivery formulation, Cormier *et al.* does not teach or suggest all of the limitations of the rejected claims and the missing claim limitations are not supplied by a secondary publication as required by MPEP § 2142.

The Examiner then draws the conclusion that since Cormier *et al.* discuss tamoxifen and raloxifene in a list of pharmaceuticals that encompasses a multitude of unrelated drug

classes that it would be obvious to one of skill in the art to combine any pharmaceutical having antiestrogenic properties with the transdermal delivery formulation claimed without regard to the pharmaceutical's chemical properties. By performing an additional database search, the Examiner located Ke *et al.* that discusses a combination therapy for the treatment of osteoporosis. Ke *et al.* mentions several drugs such as droloxifene, raloxifene, and tamoxifen and also separately mentions lasofoxifene in claims 1 and 2. From this disclosure, the Examiner asserts that it would be obvious to combine Cormier *et al.* and Ke *et al.* to arrive at the formulations and methods of the rejected claims. This conclusion, however, fails to account for the fact that transdermal drug delivery formulations similar to those claimed are not mentioned in either publication. The Examiner also fails to take into account the chemical properties of the pharmaceuticals and how these properties dictate the formulation of a substance. As a result, the Examiner's conclusion is based on the false assumption that drugs of the same pharmacologic class possess similar chemical properties and characteristics. However, this assumption is incorrect because the pharmacological classification is only based on their similar behavior in the human body and not their chemical make-up. These differences are further evidenced by the differing chemical structures and functional groups composing the pharmaceuticals that affect such properties as the stability of the active ingredient, stability of the adjuvant in combination with the active ingredient, phase distribution within the matrix, pH, and release from the matrix and bioavailability.

To support an understanding of how these pharmaceutical substances are structurally different and how their behavior in matrix systems cannot be equated, the following table shows the chemical structure of the compounds cited by the Examiner.

Pharmaceutical Name	Chemical Structure
Lasofoxifene	
Droloxifene	
Raloxifene HCl	
Tamoxifen citrate	
Idoxifene	



This diverse group of compounds naturally have differing chemical properties that affect formulation as each compound has differing functional groups (e.g. piperidine, pyrrolidine, thiophene, phenol, carboxylic acid and halogenated aromatic groups). These functional groups impart variable characteristics such as stability of the active ingredient in the matrix system, stability of the adjuvant in combination with the active ingredient, phase distribution within the matrix, pH, and release and bioavailability characteristics that would require consideration in formulating the transdermal system as presently claimed.

In addition, Ke *et al.* does not does disclose transdermal drug delivery formulations that are at all similar to those claimed by the applicants, thereby failing to suggest combining the cited publications. For example, Ke *et al.* state that "[f]or purposes of transdermal (e.g., topical) administration, dilute sterile, aqueous or partially aqueous solutions (usually in about 0.1% to 5% concentration), otherwise similar to the above parenteral solutions, are prepared" (see column 37, lines 49-52). This disclosure demonstrates that topical transdermal administration is performed using a solution. This disclosure does not demonstrate a transdermal delivery formulation containing a matrix, a hydroalcoholic gel or a liquid reservoir from which lasofoxifene is continuously released providing systemic bioavailability. Nor does, Ke *et al.* mention or consider any of the factors that must be taken

into account when formulating pharmaceuticals for transdermal delivery as presently claimed.

With these considerations in mind, one of ordinary skill in the art would not be motivated to combine the publications as the Examiner has suggested because the compounds above would be expected to have dramatically different chemical properties requiring unique formulations that may not be conducive to formulation in a drug matrix, hydroalcoholic gel or liquid reservoir. In fact, the differing chemical structures and properties of tamoxifen and raloxifene as compared to lasofoxifene actually teach away from combining lasofoxifene with the transdermal delivery system discussed in Cormier *et al.* because the compounds are so different that one of ordinary skill would not reasonably expect them to behave in the same manner when formulated into a drug matrix.

As a result, the Examiner has not set forth a *prima facie* case of obviousness because a motivation has not been defined in the art, there is no discussion of how one of skill would have a reasonable expectation of success, and the publications simply do not teach all of the claim limitations of the current claims. The very fact that the examiner has only identified some of the claimed elements in the publications demonstrates that these arguments are not sufficient to negate patentability. Accordingly, since the rejection has been overcome, it is respectfully requested that this rejection be withdrawn.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 50-2518 and notify Applicant's Attorney.

Respectfully submitted,

September 6, 2006

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